



## Review Article on Pharmaceutical Analysis of Pharmaceutical Industry According to Pharmacopoeias

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### ABSTRACT :

The pharmaceutical pill should meet specific standards to assert it as a typical drug approval. Pharmaceutical industries take a look at the tablets for maintaining their accuracy following totally different normal parameters like identity, strength, quality, purity, and stability, etc. For what why, it's essential to manage pharmaceutical processes in spite of the problems that will be addressed. Method management includes inspecting raw materials, dominant processes, and targeting for the finished product. That's why it's important to watch the effectiveness of the method management. In association to the present, the variation of the assembly method ought to suits the specification pro re nata, which can additionally embrace management of apparatus and atmosphere. Pharmaceutical merchandise within the method ought to be checked suitably for his or her identity, strength, quality, and purity and therefore the merchandise area unit approved or rejected by the standard management unit throughout the producing method. The highlights of this review area unit to explain internal control testing of pharmaceutical merchandise by victimization totally different instruments for the pharmaceutical business, in keeping with pharmacopoeias.

**Keywords :** Finished product, purity, pharmacopoeias, Rawmaterial, Quality control,

### Introduction :

Pharmaceutical business is one in every of the foremost regulated industries worldwide as a result of the medication created should be safe and effective. The Food and Drug Administration (FDA) needs that raw materials area unit tested before producing pharmaceutical merchandise to ascertain their identity, purity, and quality. This analysis is a necessary step within the production of prescription drugs and ensures that the merchandise is appropriate for its meant use. Our capabilities embrace testing raw materials, Active Pharmaceutical Ingredients (APIs), excipients, and numerous additive primarily based finished merchandise, together with u. s. formulary (USP) /National Formulary (NF), Japanese Pharmacopoeia (JP), European Pharmacopoeia (EP), Food Chemical Codex (FCC) and British Pharmacopoeia (BP). Quality isn't associate degree accident; it's the results of smart efforts [1]. Synthesis and also the properties and properties of such molecules, called active pharmaceutical ingredients (APIs), and their analysis and therapeutic efficaciousness knowledge area unit stipulations for drug candidate identification [2]. The regulatory agency permits trials once passing pre-clinical tests for clinical trial on the projected system drug. The check{test|trial|run} test produces statistically vital knowledge on the association of the drug's risky performance, safety, and overall profit. At an equivalent time, the drug is functioning on the projected system, its optimum dose, and schedule. This step determines the drug's potential interaction with different medication and monitors the long-run viability of the drug. Once palmy completion of the trial, the drug involves the marketplace for patients. Numerous tips associated with chiral medication are printed that encourage the event of one compound drug for pharmaceutical manufacturers [3,4]. Registration for quality {pharmaceuticals|prescription medication|prescribed drugs} for chiral drugs was firm by the International Conference on the Harmonization of Technical necessities within the Human Use for prescription drugs Registration [5]. Quality has become a essential and sensitive issue within the pharmaceutical business. Because the World Food and Drug Administration (FDA) for the 21<sup>st</sup> century has close to introduce, apply and guide and integrate the present smart producing System (cGMP), there's associate degree increasing awareness of the importance of pharmaceutical merchandise. Pharmaceutical finished merchandise might contain particles of unknown foreign substances [6]. Foreign problems ought to be known, and its supply ought to be outlined to stop more contamination. Within the pharmaceutical business, it's essential to regulate the defects at each stage of the producing method. The whole quality of the merchandise should be ensured in line with the mixture of the drugs [7]. Producing practices that end in the assembly of excellent quality finished merchandise and adequate issues to guard staff area unit recognized pretty much as good producing apply (GMP). GMP is related to each production and internal control (QC) [8]. QC is that the a part of GMP whereby QC workers analyzes the standard of all factors concerned in production to get rid of defects at every stage of production. The aim of QC is to provide an ideal finished product by preventing defects at every stage of production. QC is cooperation, and that we should bear in mind that quality should be created as a drug product once coming up with a product and method. It's wedged by physical plant style, placement, ventilation, cleanliness, and sanitation throughout routine production [9]. In method internal control testing is performed at regular time intervals throughout the producing process [10]. The objectives of the IPQC embrace observation and modifying the assembly method to confirm compliance with the necessities. The method management will involve the surroundings still as instrumentation management. They ought to not take any risk of product quality. The method helps characteristic the issues within the check simply. It typically identifies a defective product batch that may be repaired, however once this batch is finished contrariwise it's going to not be attainable. Failure to satisfy the IPC specification indicates that either those procedures weren't followed or that some factors were out of control [11]. Commonplace operative procedures (SOPs) ought to be established

within the pharmaceutical business, so IPQCs and tests area unit described[12.]The highlight of this review is to indicate the standard parameters of pharmaceutical analysis in line with pharmacopeias, that area unit a part of the raw materials and finished product for internal control tests.

- **Pharmaceutical Analysis for Quality Control Testing in Pharmaceutical Industry**

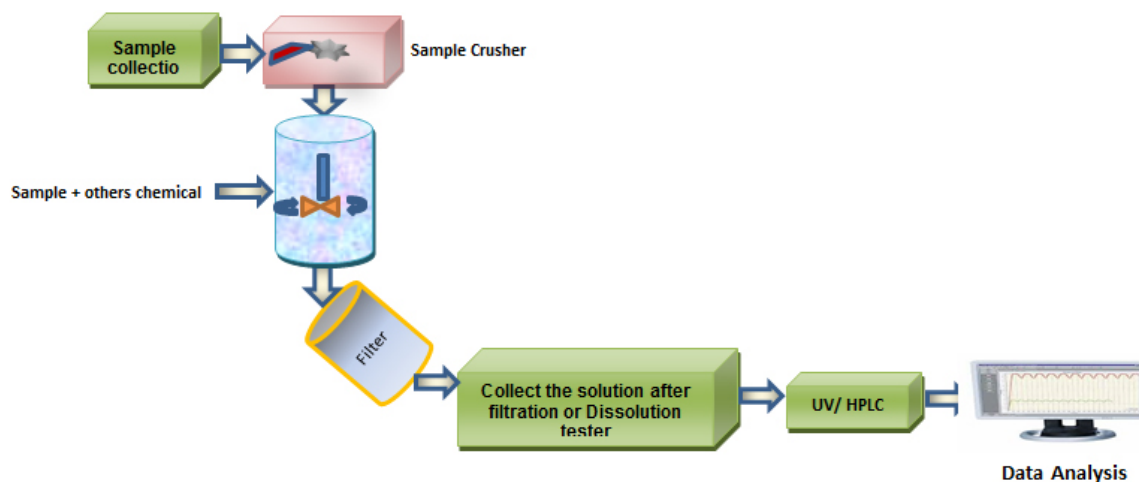
The evaluation of pharmaceutical raw materials and finished products for impurities and degradation products is an essential part of the process of drug development and production. Furthermore, toxicity data must be found on any drug-related impurities that represent a concentration of more than 0.1% of the active pharmaceutical ingredient (API). Conventional analysis of pharmaceutical QC and production fields has traditionally been performed by titration, Identification, Loss on drying, sulfate ash, dissolution, and disintegration test by using UV-visible, HPLC, GC, or IR detection.

- **Identification:**

The purpose of identification testing is to verify the identity of the active pharmaceutical ingredient (API) on the pharmaceutical pill. The identification check are going to be able to discriminate between compounds of nearly connected structures that ar in all probability gift. Identification tests ought to be specific to new drug substances, for instance, spectrum.

- **Assay:**

Specific, stability-indicating assay check to see the strength (content) of the API in pharmaceutical tablets. In several cases, it must apply constant technique (for example, actinic ray / HPLC area unit shown in figure 1) for each the drug substance and therefore the range of impurities.



**Figure 1: Schematic representation of Assay**

Chromatography and qualitative analysis area unit orthogonal techniques which means that each varieties of technique offer completely different and specific data. Action could be a quite separation technique and qualitative analysis could be a technique that offers a ‘fingerprint’ to individual or molecular mixtures. HPLC could be a technique that assist for separation, quantification, and part detection in mixtures. It’s particularly appropriate for compounds that aren’t simply volatile, aren’t thermally unstable, and have high mass. The benefit of actinic ray technique over HPLC technique is that actinic ray technique doesn’t typically need elaborate treatments and procedures associated with natural action technique. It’s time intense and economically low. The HPLC associated actinic ray spectroscopy technique is an adequate technique of measurement a drug in pure type and its dose. As a result of these ways area unit easy, fast, precise and correct, they will be with success and handily adopted for internal control analysis of medication within the kind of bulk and pharmaceutical doses on a routine basis.

Assay and Content Uniformity

Drug Impurities Analysis

Drug discovery & Drug development

Method Development and Validation of Drugs

- **UV Absorption Spectroscopy Analysis for Pharmaceutical Industry**

- **Detection of Impurities:**

UV absorption chemical analysis for crucial impurities in organic molecules is one amongst the simplest strategies. Additional peaks may be monitored

for impurities stay within the sample and might be compared with commonplace raw materials. Impurities also can be detected by mensuration absorption at specific wavelengths. For instance, aromatic hydrocarbon seems as a typical impurity in cyclohexane. Its presence is definitely detectable by absorbance of 255 nm.

#### Quantitative Analysis

The ultraviolet radiation spectrum may be wont to quantitatively verify the compounds that absorb ultraviolet radiation radiation. This determination relies on the law of brewage as below

$$A = \log I_0 / I_t = \log 1 / T = - \log T = \text{first rudiment} = \epsilon bc$$

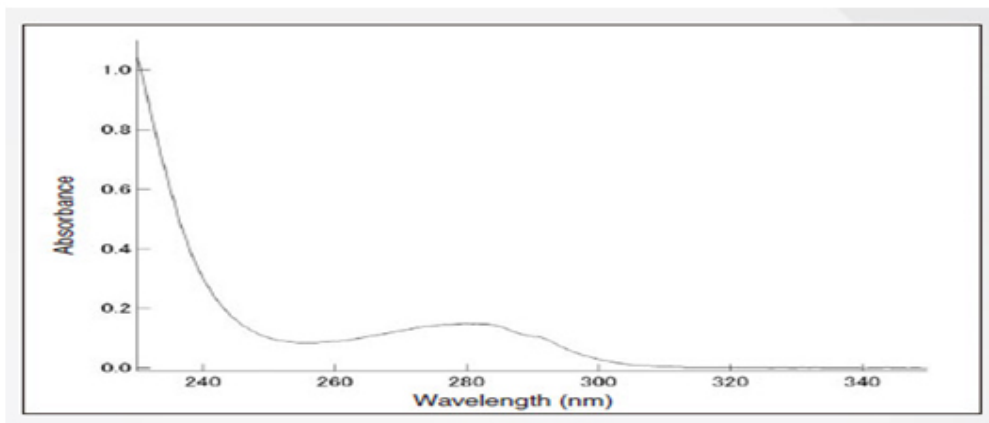
Where wherever is extinction co-efficient, c concentration, and b is that the length of the cell used on the ultraviolet radiation photometer. Ultraviolet radiation-3000 UV / Vis photometer with a one cm match quartz cell to holographic grating system, discovered lightweight of the instrument is reduced and also the analysis occur a lot of correct. Pharmaceutical product is additionally glorious for its stable performance by victimisation ultraviolet radiation / Vis photometer.

#### Qualitative Analysis

UV absorption spectrum analysis will determine the categories of compounds that absorb actinic ray radiation. The spectrum is known by examination the spectrum of the well-known compound. The actinic ray spectrum is often accustomed determine aromatic compounds and aromatic olefins

#### Quantitative Analysis of Pharmaceutical Substances:

Drugs can be both in the shape of uncooked substances or in formulas. These can be synthesized with the aid of growing terrific drug options in the solvent and measuring absorption at precise wavelengths is proven in discern two The Diazepam pill can be analyzed by using methanol through 0.5% H<sub>2</sub>SO<sub>4</sub> at wavelength 257 nm. Qualitative evaluation via spectrophotometric strategies yields quick and correct effects the use of solely small pattern volumes. This quick and environment friendly fabric has end up an necessary device in the pharmaceutical industry, thanks to its adaptability and monetary value. Qualitative evaluation has confirmed to be surprisingly positive at many massive stages of natural compounds and this helps to make sure the fitness and protection of the patient.

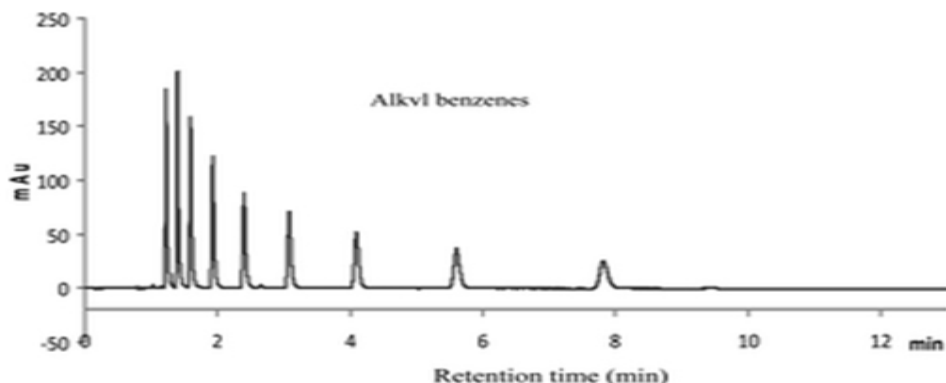


**Fig.2: UV Absorption spectroscopy Analysis**

- **High-Performance Liquid Chromatography Analysis for Pharmaceutical Industry**

High-performance liquid action (HPLC) could be a activity analytical technique accustomed split a mix of chemistry, organic chemistry and industrial field compounds. The most purpose for exploitation HPLC is to purify the quantities and blend individual parts. Since it's accustomed take a look at product and establish the stuff, it's additionally accustomed perform qualitative and mensuration of their product. HPLC plays a major and demanding role within the pharmaceutical business and analysis. Associate degree HPLC instrument includes a pump, injector, column, and detector and knowledge acquisition and show system. It will observe little amounts of solvent & improved resolution of the compound from the column. What is more, the importance of HPLC during this field is subject to demanding rules established by the Food and Drug Administration (FDA) within the us. In line with the USA accumulation (1999), 14th the HPLC technique established for the primary time the trial of bulk drug materials. It makes analytical support inside the pharmaceutical industry[15] become the popular technique of internal control and assurance at several levels. Additionally to HPLC analysis of the medicine and its application to impurities analysis of the prescribed drugs has Been applied[16,17.]All these pharmaceutical corporations apply this required technique HPLC to spot the standard of their product before permitting them to be sold-out in international markets. The foremost vital advantage of exploitation HPLC technique within the business and analytical field is that it helps to elucidate the structure and quantitative determination of impurities and degradation product in massive quantities of drug materials and pharmaceutical composition. This edges from the utilization of HPLC is restricted not solely to artificial medicine and formulas however additionally to incorporate flavourer medicines too. Drug discovery, development, and production utilize wide used high performance liquid action (HPLC) to separate individual compounds for the

detection, quantification, and purification of various parts. Schematic illustration of HPLC analysis area unit shown in figure three Thus, there's a good demand for HPLC instruments for advanced analysis of the "next generation" detection. Monica Young and Mark at Eksigent



**Figure 3: High-performance liquid chromatography Analysis**

Corporation have tested the effectiveness of Eksigent specific LC radical Micro-High-Pressure Liquid action for a real-world pharmaceutical application. By combining the aptitude of micro-flow HPLC, and also the operate to separate beneath high pressures, the new instrument permits quick separation potency, value reduction and high system reproducibility[18]. Most staff use reverse-phase mode with ultraviolet light absorption detection once acceptable, as a result of it provides the most effective on the market dependability, analysis time, repeatability and sensitivity. HPLC has been utilized in many pharmaceutical drug makers [19-22] and biological fluids[ 23-26]. As such, HPLC provides a superb service in respondent several of the queries raised by the pharmaceutical business. However, the restrictions of HPLC lack the semipermanent duplicability thanks to the proprietary nature of column rating, solvent and column packing. Liquid action combined with mass qualitative analysis (LC-MS) is taken into account to be one in all the foremost vital analytical technique of the last decade of the twentieth century twenty seven. The pharmaceutical business has become the well-liked methodology for internal control and analytical support at several levels of assurance[ 28-29]. HPLC-MS has recently been used for medication [30-36. ]HPLC medication are applied for the analysis of medication alone, still as for the prescription drugs [37-41 ]and also the impurity merchandise forty two – forty four.

- **Impurities**

Organic as nicely as inorganic impurities and residual solvents are included in this Section. This test determines the presence of any component that is not API or an Excipient to pharmaceutical products. The most frequent types of impurities that Are measured are related substances, which are impure processing of new drug Substances, API degradation products.

NA

- **Raw Materials and Finished Product Test for Pharmaceutical Industry**

The physical parameters test of raw material for the pharmaceutical industry are temperature, pressure, moisture content, weight, particle size, hardness, loss of drying, sulfate ash, color, integrity. Test of the finished product for pharmaceutical industry are assay, Uniformity of content, uniformity of mass, weight variation, friability test, content of active ingredients, hardness test, disintegration test, dissolution test etc. The raw materials and finished product tests for the pharmaceutical industry according to pharmacopoeias are listed below :

**Size and Shape**

The size and shape of the tablet can be described dimension-ally and controlled. This is determined by the equipment during the condensation process[13]

**Color and Odor**

Many pharmaceutical tablets use color as an essential means of quick identification and consumer acceptance. But it certainly equates to a lot in a single tablet, from tablet to tablet and lot. The presence of odor in a batch of tablets may indicate stability issues such as. Vitamins may have a characteristic odor, for example, the characteristic odor of acetic acid or the drug's ability to degrade aspirin tablets. Flavor tablets are important in customer acceptance[13]

**Moisture Content of Granules**

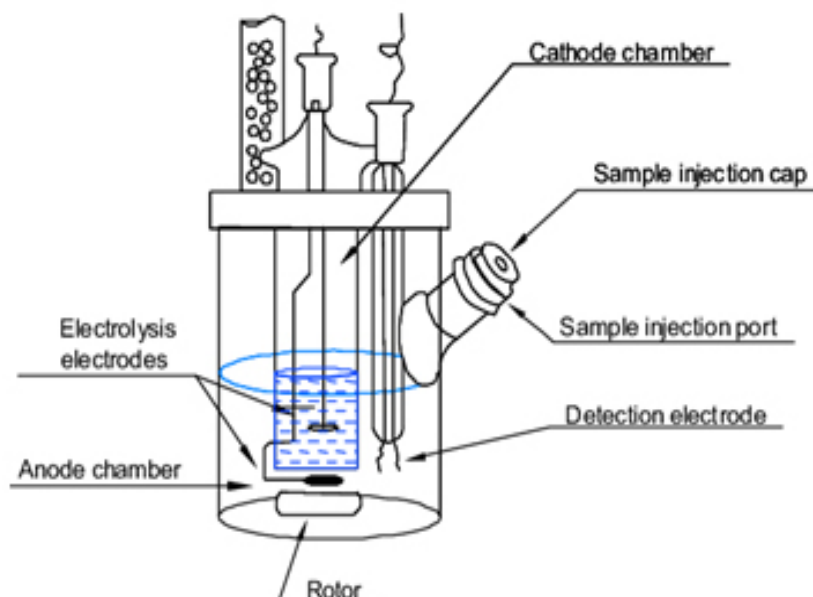
The granules should have enough strength to not break a large amount of fine powder and prevent normal handling and mixing processes. On the other hand, it is wise to expose some areas of clear surfaces for optimal bonding while reducing the size of the connections on the tablets, so moisture content is very important for producing good drug products[37]

- **Assay**

A tablet contains an active ingredient called API. So in order to be able to make the tablet well finished product relations production has to be done using proper analysis method[13]

- **Water content:**

Acceptance criteria may be justified with information on the effects of hydration or water absorption on drug products. In some cases, a loss may be considered sufficient in the drying process; however, there is an identification method that is specific for water (e.g., Karl Fisher titration) are shown in figure 4. Many active pharmaceutical ingredients (APIs) and adjuvants are water or bound in an adsorbed form (surface water) called hydrate. The water content of drugs strongly affects their quality, shelf life and durability as well as the release of active substances. Water determination is therefore an important assumption in pharmaceutical analysis. By far, the most important method for determining the water content of drugs is Karl Fisher titration. The Karl Fisher oven method is suitable for samples that simply release their water at high temperatures, difficult to dissolve or react with KF reagent. Sample preparation is very easy. The material to be analyzed is loaded into a sample vial, which is hermetically sealed with a septum and placed on a rack. Heat the sample in an oven and release water from the sample. A double blank needle pores the septum and a stream of carrier gas transports moisture to the titration cell for subsequent determination.



**Figure 4: Karl Fisher titration (<https://images.app.goo.gl>)**

- **Uniformity of Content**

A physically protected tablet may not produce the desired effect. To evaluate tablet potential for efficacy, it is necessary to monitor the amount of drug per tablet, from tablet to tablet, and from batch to batch. For this test according to BP using the appropriate experimental analysis method, determine the individual content of active substance of 10 tablets taken at random[36]. The tablet complies with BP-based testing, if the average content of each individual content is 85 percent to 115 percent. If the tablet fails to comply with the test, more than one distinct content is out of range or if one individual content is out of the range the average content is 125 percent to 75 percent. If an individual content exceeds the 85 percent to 115 percent limit, set the individual content of the other 20 tablets taken randomly, in the range of 75 percent to 125 percent. The tablet agrees with the test if no more than 30 tablet-specific content is out of the range of 85 percent to 115 percent of the average content and nothing is out of the range of 75 percent to 125 percent of the average content[37].

### Microbial limit

Microbial limit is seen as a feature of experimental good manufacturing Practice, as well as quality assurance. In general, it is advisable to test the product of the drug unless its ingredients are tested before production and the manufacturing process is informed, through validation studies, not carrying a significant risk of bacterial infection or outbreak. It should be noted that this guideline does not directly address externalities, but the policies outlined here may apply to outsiders as well. In both cases, skip testing can be an appropriate method. With acceptable scientific justification, it may be possible to suggest a microbial limit test for powders intended for reconstitution as oral liquids.

### Uniformity of dosage units

This time period includes each the mass of the dosage form and the content material of the active substance in the dosage form; a pharmacopoeia strategy should be used. In general, specs should consist of one or the other, but now not both. If appropriate, this can be edited in the testing process. Acceptance standards should be covered in the specification. When applying weight editions to new drug products in pricing, candidates should confirm that the homogeneity of the product is sufficiently sufficient when growing the drug.

### Weight Variation Test

According to the USP Weight variation test, up to 20 tablets are independently run by comparing average weight and average individual tablet weight. Weight loss tests are manifested in percentages. The following formulas are used:

Weight Variation =  $(Iw - Aw) / Aw \times 100\%$  where,  $Iw$  = Individual weight of tablet;  $Aw$  = Average weight of tablet[28].

According to the USP, the tablet agrees to the test if the individual population has no more than 2 percent deviations from the average mass, as shown in Table 1, and no more than twice the percentage[38]

Table 1: USP limits for weight variation test for uncoated tablets

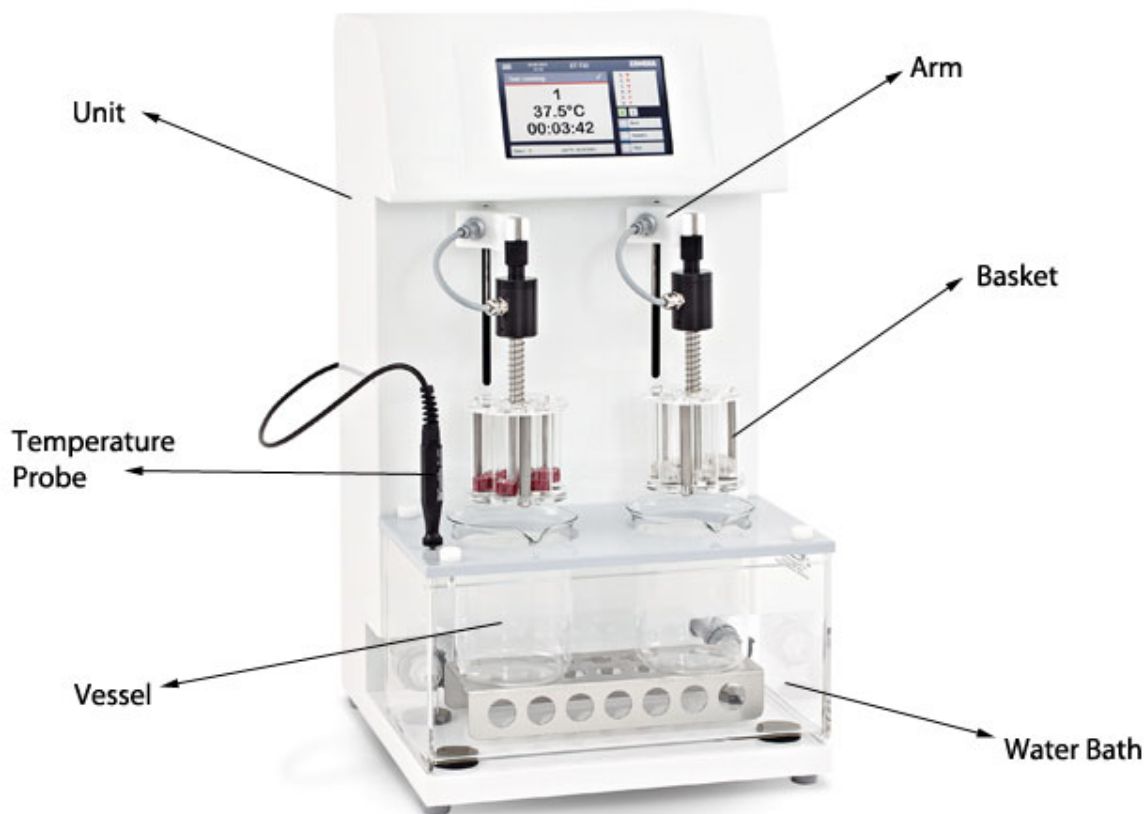
Average Weight (mg)	Percentage Deviation (%)
130 or less	10
130-324	7.5
More than 324	7

- **Hardness Test**

One of the early testers for this test was the Ketan Tablet Hardness Tester, a type of Monsanto hardness tester for evaluating the tablet hardness tester. The tester has a barrel. Lower plunger is kept in touch with tablet and zero read is taken. The threaded bolt is forced against a spring until the upper plunger enthusiast cracks the tablet. As the spring narrows, a pointer moves with the barrel gauge to indicate the ball. The force of the crack is recorded in kilograms. It is naturally appropriate to examine the rigidity as a procedural control. In these situations, it is usually not necessary to include these features in the specification. If the hardness characteristics have a serious impact on the quality of the product of the drug (e.g., chewable tablets), the standard of recognition should be included in the specification[38].

- **Disintegration Test**

The USP disintegration instrumentation consists of six glass tubes that are three inches long, open at the highest, and placed at the backside finish of the



basket rack assembly con to the 10-mesh screen, with one pill placed on each tube, and therefore the basket rack mounted at medium  $37 \pm 0.5$  a pair of  $^{\circ}\text{C}$  such pills ar placed a pair of .5 cm below the surface of the fluid at their upward motion and therefore the vessel descends nearer than a pair of .5 cm from very cheap A general motor-driven device is employed to maneuver the basket meeting with tablets at distances of five to six cm at a frequency of twenty eight to thirty two cycles per minute. Perforated plastic disks may be utilized in the tests. These ar positioned on prime of the tablets and grant a harmful action on the tablets. Whereas disks will be important or produce a lot of sensitivity to tests, they're helpful for floating tablets. Operate the machine for a set time (15 minutes for uncoated tablets till otherwise even and approved) forty seven. The pill complies with the take a look at, if the tablets ar disconnected and every one particles pass via the 10-mesh screen at the desired time. If any residue is left, it got to have a soft mass that has no clear firm core. The pill complies with the experiment in step with USP, if all capsules ar utterly disconnected. If one or a pair of medicine fail to interrupt utterly, repeat the take a look at on twelve additional tablets. Total eighteen tablets not abundant but sixteen however the requirements ar met to check land accumulation (BP) and Indian accumulation (IP) limits for disintegration times of medication ar given in Table a pair of, Table three and shown in recognise five respectively[38].

**Table 2: BP limits for disintegration times of tablets**

Categories of Tablets	Disintegration Time (min)
Uncoated tablets	15
Coated tablets.	60
Effervescent tablets	5
Soluble tablets	3
Dispersible tablets	3
Oro dispersible tablets	3
Gastro-resistant tablets	60
Oral lyophilisates	3

**Table 3: IP limits for disintegration times of tablets**

Categories of Tablets	Disintegration Time (Min)
Uncoated tablet	15
Coated tablet	60
Enteric-Coated tablet	60
Film-coated tablets	30
Effervescent tablet	5
Soluble tablets	3
Dispersible tablets	3

**Table 4:Usp limits for disintegration times of tablets**

Categories of Tablets	Disintegration Time (Min)
Uncoatedtablet	5
Coatedtablet	60
Enterictablet	60
Film -coatedtablet	30
Effervescenttablet	5
SolubleTablets	3
Dispersibletablet	5

- Dissolution Test**

BP or USP dissolution apparatus (paddle / basket apparatus) consist of a cylindrical vessel with a hemispherical bottom, which may be covered with glass or other inert, transparent material; a motor; a metal drive alloy; and a cylindrical basket are shown in figure 6. The vessel is partially immersed in a convenient water bath of a convenient size or heated by a suitable device such as a heating jacket. A water bath or heating device allows the temperature inside the vessel to be kept at  $37 \pm 0.5$  ° C during the test and keeps the bath fluid in constant, smooth motion. According to BP, keep the specified volume ( $\pm 1$  %) of the dissolution medium in the vessel for this test<sup>46</sup>. Assemble the apparatus, adjust the dissolution medium to  $37 \pm 0.5$  ° C. Carefully remove 1 of the air bubbles from the surface of the tablet. Operate the apparatus at a fixed rate. Within a specified time interval, or each time specified, withdraw a sample from the zone of the midway between the surface of the dissolution medium and the top of the rotating basket, not less than 1 cm from the wall of the vessel. Where multiple sampling times are specified, replace the withdrawn aliquots at 37 ° C for newly dissolution medium or, where it can be shown that the medium does not need replacement, is correct for volume changes in the calculation. Keep the vessel covered for the duration of the test, and at a suitable time, check the temperature of the medium. Perform analysis using appropriate side procedures as directed by individual monographs. Repeat the experiment with additional tablets. Unless specified otherwise in separate monographs, 5the amounts of active ingredient dissolved in the tablets tested from the tests required by British Pharmacopoeia(BP), United States Pharmacopoeia (USP), European Pharmacopoeia (PhEur), Japanese Pharmacopoeia(JP) and International Pharmacopoeia (PhInt) meet the following recognition criteria are show in table 4.

Table 4: BP, USP, PhEur, JP and PhInt acceptance criteria for dissolution test of tablet

Stage	Number of Tablet Tested	Acceptance Criteria
S1	6	Each unit is not less than $Q + 5$ %.
S2	6	Average of 12 units (S1 + S2) is equal to or greater than Q, and no unit is less than $Q - 15$ %.
S3	12	Average of 24 units (S1 + S2 + S3) is equal to or greater than Q, not more than 2 units are less than $Q - 15$ %, and no unit is less than $Q - 25$ %.

If the results are not consistent with S1 or S2, continue the experiment in phase 3 Quantity Q, is the specific amount of dissolved active substance, expressed as a percentage of the labeled material; the 5 percent, 15 percent, and 25 percent values in the table are the percentage of content labeled so that these values and Q are in the same terms [39]

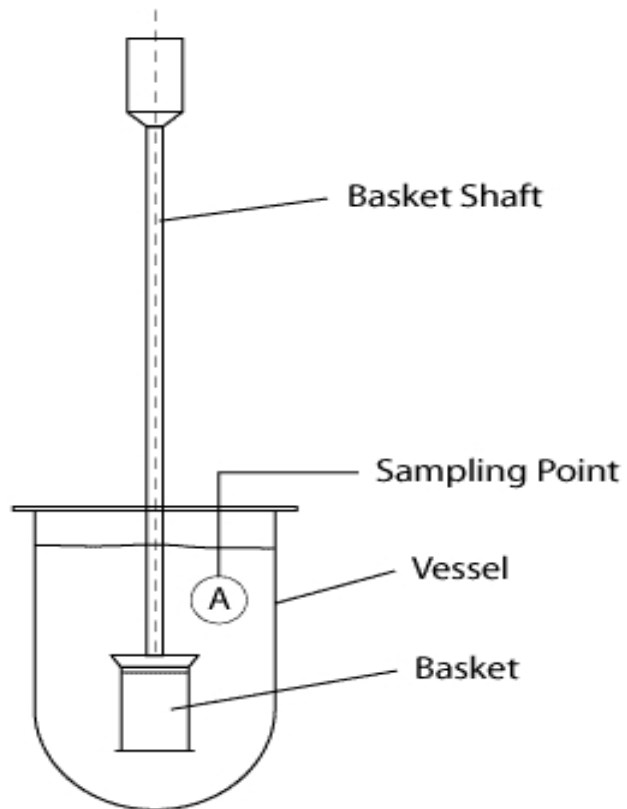




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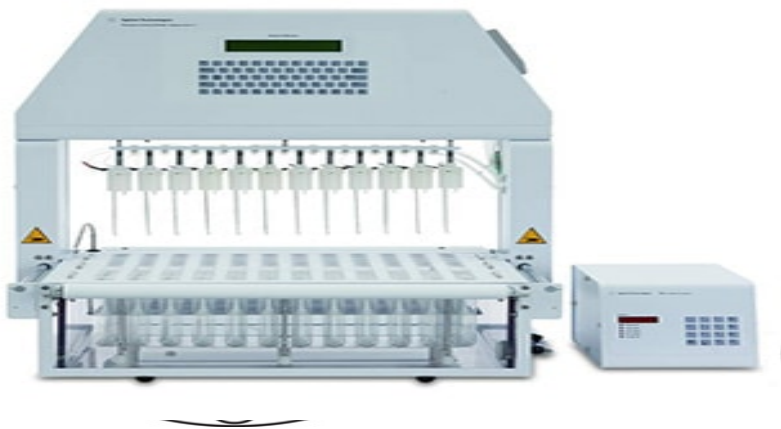
### Types of dissolution Apparatus:

1. **Basket type** :It comprises borosilicate glass and holds capacity up to 1000m .the common speed limit is 100rpm.

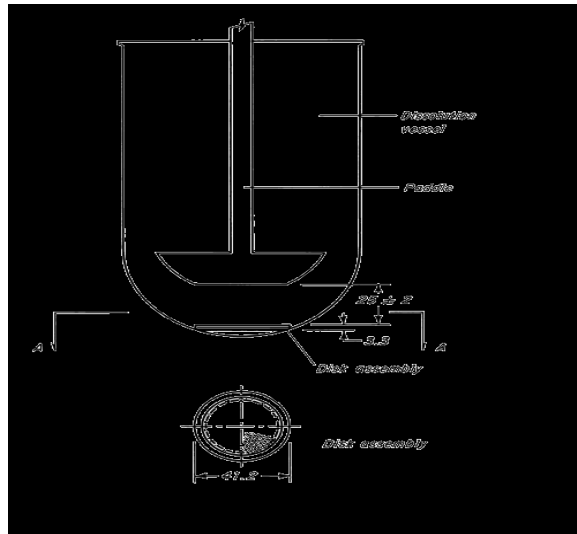


**2.Paddle type** : this paddle is designed from stainless-steel.It has motor speed 50 rpm for capsule and 25rpm for suspensions.

**3.Resiprocatingcylinder**:It is an easy method for testing .



**4.Flow through cell** :Flow rate ranges from 4 to 16 ml/min. six samples are tested during the dissolution testing. And the medium is maintained at 37°C.



**5. Paddle over the disk :** Its volume capacity is 900ml. The paddle over disk assembly is used for the dissolution testing of transdermal patches, is offered in a variety of sizes, and is used with a standard dissolution apparatus.



**6. Rotating cylinder:** The rotating cylinder assembly uses a stainless steel cylinder and includes four slots at the top for improved media circulation. Each rotating cylinder includes two sizes, one for smaller patches, the other for larger ones.

**7. Reciprocating disc:** Typical products tested include extended release tablets, capsules, transdermals, osmotic pumps, and arterial stents.

**CONCLUSION:**

The main goal of pharmaceutical products is to serve human beings to protect them from potential illness or disease. The drug should be free from impurities or other interference to fulfill its intended purpose, which can harm people. Pharmacopoeias sets the standard for high quality drugs. According to the WHO list, 140 independent countries currently employ around 30 national and African, European and international pharmacopoeias. From present study, it is clearly expressed that various pharmacopoeias suggest different types of raw materials and finished products test for pharmaceutical tablet using different instruments in the pharmaceutical industry, but the main purpose of pharmacopoeias worldwide is to produce good quality drugs for human health.

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